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DECEMBER 2021 BIOSIMILAR PIPELINE REPORT

DID YOU KNOW?

"Interchangeable" Biosimilars

Upwards of 30 biosimilars have been approved by the FDA since the first one was approved in 2015; yet until mid-2020, no biosimilar had been approved as interchangeable with its reference product. In June of last year, however, the FDA approved Semglee, a biosimilar for Lantus insulin, as interchangeable; and this edition of the Biosimilar Pipeline Report introduces Cyltezo, the second approved interchangeable biosimilar (reference product, Humira). But what is the difference between biosimilars that are interchangeable with their reference products, and ones that are not? The answer to that question boils down to two related factors: First of all, interchangeable biosimilars have had additional testing to demonstrate equal safety and effectiveness to their reference products in patients who have switched back and forth between the biosimilar and its reference product. This evidence lays the groundwork for the second factor: interchangeable biosimilars may be substituted for their reference products at the pharmacy, without the involvement of the prescriber (as long as state laws permit this). In this way, interchangeable biosimilars resemble generics of non-biologic drugs; and as with generics, this process will help health plans and their members to save on these drugs without having to work through the prescriber.

The FDA emphasizes that interchangeable biosimilars have not been shown to be safer or more effective than non-interchangeable ones. But if interchangeability becomes the norm for biosimilars, pharmacies may be able to limit their stock of brands and/or negotiate reduced prices for biosimilars by bidding interchangeable biosimilars against each other. This should in turn drive increased competition and reduce costs for biologic drugs over the long run.

Recent Developments

- A biosimilar for Eylea (aflibercept, a product that reduces symptoms of retinal disorders) is in development. This reference product is new to our list, having previously had no other biosimilars, approved or not.
- The second interchangeable biosimilar has been approved (see story above for more information). Cyltezo, referenced to Humira, was approved in 2017 but was only recently granted interchangeable status.
- There have been no new biosimilar launches since the last edition of the Biosimilar Pipeline Report, and only one new approval (Byooviz, referenced to Lucentis)

New Biosimilars in Development

- **BEVZ92** - referenced to Avastin
- **MYL-1701P M710** - referenced to Eylea
- **FYB201 CHS-201** - referenced to Lucentis
- **Yuflyma** - referenced to Humira
- **Lupifil-P** - referenced to Neulasta
- **TPI-120** - referenced to Neulasta
- **FKB238** - referenced to Avastin

Orange boxes denote launched products

Approval Date	Launch Date	Biosimilar Name	Interchangeable	Biosimilar WAC/ Year Cost	Reference Product	Reference Product WAC/ Year Cost	Disease Category**
9/14/2017	7/18/2019	**Mvasi** (bevacizumab-awwb) Amgen Allergan	No	$127,330.25	**Avastin** (bevacizumab)	$145,270	**Cancer**: Treatment of metastatic colorectal cancer, non-squamous non-small cell lung cancer, glioblastoma, metastatic renal cell carcinoma, persistent, recurrent, or metastatic carcinoma of the cervix.
6/27/2019	12/31/2019	**Zirabev** (bevacizumab-bvzr) Pfizer	No	$111.945.50			
Estimated 2Q2022	**Estimated** 2023	**BEVZ92** mAbxience; Insud Pharma; Amneal		**TBD** Upon Launch			
Estimated 12/27/2020	**Estimated** 1H2021	**Bmab-100 Apollo;** MYL-1402O Biocon Mylan		**TBD** Upon Launch			
Estimated 1H2021	**Estimated** 1H2021	**SB-8** Merck Samsung Bioepis		**TBD** Upon Launch			
Estimated 11/27/2021	**Estimated** 4Q2021	**BAT1706** Bio-Thera Solutions		**TBD** Upon Launch			
Pending	**Estimated** 2021	**FKB238** Centus Biotherapeutics; AstraZeneca; Fujifilm Kyowa Kirin		**TBD** Upon Launch			

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8/30/2016	**Estimated** 2028-2029	**Erelzi®** (etanercept-szzs, aka GP2015) Sandoz	No	**TBD** Upon Launch	**Enbrel** (etanercept)	$77,799	**Immunosuppressant**: Ankylosing spondylitis, juvenile idiopathic arthritis (2 years or older), plaque psoriasis adult, psoriatic arthritis, rheumatoid arthritis.
4/25/2019	**Estimated** 2028-2029	**Eticovo** (etanercept-ykro, aka SB4) Samsung Bioepis	No	**TBD** Upon Launch			
5/15/2018	11/14/2018	**Retacrit™** (epoetin alfa-epbx) Hospira Pfizer Vifor Pharma	No	$11,471.43	**Epogen** **Procrit** (Epoetin Alfa)	**Epogen AND Procrit -** $17,290.57	**Hematopoietic**: Treatment of anemia due to chronic kidney disease, zidovudine in hiv-infected patients, chemotherapy in cancer patients, and reduction of allogeneic red blood cell transfusion in patients' elective surgery.
Estimated 4Q2022	To Be Determined	**MYL-1701P M710** Momenta; Mylan; Janssen; Viatris	No	**TBD** Upon Launch	**Eylea** (aflibercept)	$12,058	**Ophthalmic product**: Reduces symptoms from disorders of the eye's retina.

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12/14/2018	03/16/2020	**Herzuma** (trastuzumab-pkrb) Nippon Kayaku Celltrion Teva	No	$68,255	**Herceptin** (trastuzumab)	$75,840	**Cancer**: Treatment of human epidermal growth factor receptor 2 (her2) adjuvant breast cancer, metastatic breast cancer, and metastatic gastric cancer
6/13/2019	7/18/2019	**Kanjinti** (trastuzumab-anns) Amgen Allergan	No	$64,262			
12/1/2017	12/2/2019	**Ogivri** (trastuzumab-dkst) Mylan Biocon	No	$64,262			
1/18/2019	04/15/2020	**Ontruzant** (trastuzumab-dttb) Samsung Bioepis Merck & Co	No	$64,466			
3/11/2019	2/18/2020	**Trazimera** (trastuzumab-qyyp) Pfizer	No	$58,940			
12/16/2020	3/4/2021	**Margenza**[1] (margetuximab-cmkb ["biobetter" of Herceptin) (IPD Analytics, 2021) MacroGenics	No	$151,621			

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11/15/2019	**Estimated** 11/20/2023	**Abrilada** (adalimumab-afzb, aka PF-06410293) Pfizer	No	**TBD** Upon Launch	**Humira** 50mg/ml (adalimumab)	$77,800	**Immunosuppressant:** Treatment of ankylosing spondylitis, juvenile idiopathic arthritis, rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, Crohn's disease, and/or ulcerative colitis
9/23/2016	**Estimated** 1/31/2023	**Amjevita™** (adalimumab-atto, aka ABP 501) Amgen	No	**TBD** Upon Launch			
8/25/2017	**Estimated** 7/1/2023	**Cyltezo™** (adalimumab-adbm, aka BI 695501) Boehringer Ingelheim	Yes	**TBD** Upon Launch			
7/23/2019	**Estimated** 6/30/2023	**Hadlima** (adalimumab-bwwd, aka SB5) Biogen Samsung Bioepis Merck & Co	No	**TBD** Upon Launch			
7/6/2020	**Estimated** 7/31/23	**Hulio** (adalimumab-fkjp, aka FKB327) Fujifilm Kyowa Kirin; Mylan; Biocon	No	**TBD** Upon Launch			
10/30/2018	**Estimated** 9/30/2023	**Hyrimoz** (adalimumab-adaz, aka GP2017) Amgen	No	**TBD** Upon Launch			

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Estimated 9/2021	**Estimated** 2023	**AVT02** Alvotech; Teva; Alvogen	No	**TBD** Upon Launch	**Humira** 50mg/ml (adalimumab)	$77,800	**Immunosuppressant**: Treatment of ankylosing spondylitis, juvenile idiopathic arthritis, rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, Crohn's disease, and/or ulcerative colitis.
Estimated 12/2021	**Estimated** 2H2023	**CHS-1420** Coherus	No	**TBD** Upon Launch			
Pending	**Estimated** 2023-2027	**AVT02** Alvotech; Teva; Alvogen		**TBD** Upon Launch	**Humira** 100mg/ml (adalimumab)	$77,800	
Estimated 2022	To Be Determined	**Yuflyma, CT-P17** Celltrion		**TBD** Upon Launch			
6/11/2020	8/31/2020	**Semglee** (insulin glargine, aka MYL-1501D) Biocon Mylan	Yes	**WAC per ml**: $9.87 (note this is not annual cost, which would vary widely between patients)	**Lantus** (insulin glargine)	**WAC per ml**: $28.35 (note this is not annual cost, which would vary widely between patients)	**Anti-diabetic**
9/17/2021	**Estimated** 6/2022	**Byooviz** (ranibizumab-nuna, aka SB11) Samsung Bioepis; Biogen	No	**TBD** Upon Launch	**Lucentis** (ranibizumab)	$24,420	**Ophthalmic product**: prevents overgrowth of blood vessels within the eye.
Estimated 8/2/2022	**Estimated** 2H2022	**FYB201 CHS-201** Formycon; Santo Holding; bioeq; Swiss Pharma International AG; Coherus BioSciences; Polpharma		**TBD** Upon Launch			

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6/4/2018	7/2018	**Fulphila™** (pegfilgrastim-jmdb) Mylan Biocon	No	$54,425	**Neulasta** (pegfilgrastim)	$83,663	**Hematopoietic**: Reduce incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
11/2/2018	1/3/2019	**Udenyca** (pegfilgrastim-cbqv) Coherus	**No**	$ 54,425			
11/4/2019	11/8/2019	**Ziextenzo** (pegfilgrastim-bmez, aka LA-EP2006) Sandoz	**No**	$ 51,172			
6/10/20	12/1/2020	**Nyvepria** (pegfilgrastim-apgf, aka HSP-130; PF 06881894) Hospira; Pfizer; Biorasi	No	$ 51,165			
Estimated 4/2022	**Estimated** 4/2022	**Lupifil-P** Lupin		**TBD** Upon Launch			
Pending	**Estimated** 2022	**TPI-120** Adello Biologics; AE Companies; Kashiv Bio-sciences; Amneal Amgen		**TBD** Upon Launch			

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Pending	**Estimated** 2H2021	**MSB11455** Fresenius; Dr. Reddy's		**TBD** Upon Launch	**Neulasta** (pegfilgrastim)	$83,663	**Hematopoietic**: Reduce incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
Pending	To Be Determined	**Lapelga Neupeg™** (pegfilgrastim, aka CHS-1701) Intas Apotex Accord		**TBD** Upon Launch			
Estimated 3/30/2022	**Estimated** 3/2022	**Ryzneuta²** (benegrastim ["biobetter" of Neulasta], aka Bineura; SPI-2012) Generon (Shanghai) Corporation Ltd; Evive Biotech		**TBD** Upon Launch			
Estimated 4/2022	**Estimated** 4/2022	**Rolontis³** (eflapegrastim ["biobetter" of Neulasta], aka HM10460A; HNK460; SPI-2012) Hanmi Pharmaceutical; Spectrum		**TBD** Upon Launch			

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8/29/2012	11/11/13	**Granix®** (tbo-filgrastim) Teva	No	$53,016.25	**Neupogen** (filgrastim)	$26,567	**Hematopoietic:** To reduce the incidence of infection in patents receiving chemotherapy, reduce the duration and time to recovery from neutropenia caused by chemotherapy, mobilization of progenitor blood cells for collection by leukapheresis, and reducing the incidence and duration of complications due to severe neutropenia.
7/20/2018	9/2018	**Nivestym™** (filgrastim-aafi) Hospira Pfizer	No	$46,628.75			
3/6/2015	9/3/2015	**Zarxio®** (filgrastim-sndz) Sandoz	No	$58,126.25			
Pending	2022	**Filgrastim Kashiv TPI G-CSF** (filgrastim) Kashiv AE Companies Amneal Adello Biologics		**TBD** Upon Launch			
Pending	To Be Determined	**Grastofil** (filgrastim) Intas Apotex Accord		**TBD** Upon Launch			

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Approval Date	Launch Date	Biosimilar Name	Interchangeable	Biosimilar WAC/ Year Cost	Reference Product	Reference Product WAC/ Year Cost	Disease Category**
Estimated 1Q2021	**Estimated** 2022	**MYL-1601D** Mylan; Biocon		**TBD** Upon Launch	Novolog Flexpen (insulin aspart)	**WAC per 5 units:** $1.86 (note this is not annual cost, which would vary widely between patients)	**Antidiabetic**
4/5/2016	11/28/2016	**Inflectra®** (infliximab-dyyb) Celltrion Pfizer	No	$21,528	Remicade (infliximab)	$26,567	**Immunological agent:** ankylosing spondylitis, Crohn's disease (fistulizing), adult, Crohn's disease, adult and pediatric (6 years or older), plaque psoriasis, psoriatic arthritis, rheumatoid arthritis in combination with methotrexate, ulcerative colitis
4/21/2017	7/24/2017	**Renflexis®** (infliximab-abda) Samsung Bioepis Merck & Co	No	$17,140			
12/6/2019	5/26/20	**Avsola** (infliximab-axxq aka ABP 710) Amgen	No	$13,650			
12/13/2017	To Be Determined	Ixifi (infliximab-qbtx; aka PF-06438179) Pfizer	No	**TBD** Upon Launch			

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Approval Date	Launch Date	Biosimilar Name	Interchangeable	Biosimilar WAC/ Year Cost	Reference Product	Reference Product WAC/ Year Cost	Disease Category**
7/23/2019	1/23/2020	**Ruxience** (rituximab-pvvr) Pfizer	No	$37,088	**Rituxan** (rituximab)	$48,611	**Cancer**: Treatment of patients with non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, granulomatosis with polyangiitis and microscopic polyangiitis.
11/18/2018	11/11/2019	**Truxima™** (rituximab-abbs) Celltrion Teva	No	$43,633			
12/17/2020	1/1/2021	**Riabni** (rituximab-arrx) (ABP 798) Amgen; Allergan; Abbvie	No	$37,088			

*CRL (Complete Response Letter) is a communication to a drug's manufacturer from the FDA indicating that the application for the drug cannot be approved in its present form.
**Indications for the biosimilars may vary from the originator and from each other, and are continually evolving. Indications listed here are for the originator product.

[1,2,3] Notes on "biobetters":

1. Margenza has been compared to its reference product, trastuzumab (Herceptin), in a study that demonstrated longer survival for patients taking Margenza.
2. Rolontis, still in development, has been compared in clinical trials to its reference product pegfilgrastim (Neulasta). So far, Rolontis has been shown NOT to be inferior to pegfilgrastim in terms of duration of neutropenia, and similar in safety.
3. Ryzneuta is also a biobetter in development with reference to pegfilgrastim. In early clinical trials it was shown to be safe and effective.

The above information was assembled from government and clinical resources for knowledge purposes only. Information and drugs were selected by clinicians based on therapy and potential clinical impact without any manufacturer affiliations or conflicts of interest. Approval status, dates, and WAC price are subject to variation. This document should not be exclusively used for decision-making purposes. WAC pricing data should be used for benchmarking purposes only. Prices listed above should not be used alone to set or adjudicate any prices for reimbursement or purchasing functions or considered to be an exact price for a single product and/or manufacturer.

REFERENCES

1. Bernstein Research. Biosimilars (Sept update): A $2.8B US business growing quickly; $5.6B US savings; Amgen and Pfizer establish a lead. Published September 16, 2020.
2. DRUGDEX® System, 2020, 2021. http:micromedexsolutions.com. Greenwood Village, CO: Thomson Micromedex.
3. IPD Analytics, 2020. https:ipdanalytics.com. Bay Harbor Islands, FL.
4. IPD Analytics. RxBrief: Drug Management, Update on Biosimilars in the United States. IPD Analytics, Bay Harbor Islands, FL. Published November 2020.
5. Amgen. (2020). FDA Approves Amgen's RIABNI™ (rituximab-arrx), A Biosimilar To Rituxan® (rituximab). Thousand Oaks, CA: PRNewswire.
6. Business Wire. (2020, October 26). Spectrum Pharmaceuticals Announces that the FDA is Deferring its Action on the BLA for ROLONTIS® (eflapegrastim). Retrieved from businesswire.com: https://www.businesswire.com/news/home/20201026005289/en/Spectrum-Pharmaceuticals-Announces-that-the-FDA-is-Deferring-its-Action-on-the-BLA-for-ROLONTIS%C2%AE-eflapegrastim
7. FDA. (2021, November 12). Biosimilar and Interchangeable Products. Retrieved from www.fda.gov: https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products#diffbiochange
8. IPD Analytics. (2020, December 17). Rituxan (Rituximab) Update: FDA Approves Third Rituxan Biosimilar. Bay Harbor Islands, FL, USA.
9. IPD Analytics. (2021). Biobetters Versus Biosimilars. Bay Harbor Islands, FL: IPD Analytics.
10. IPD Analytics. (2021, May 4). Biosimilar Launch Schedule. Retrieved from ipdanalytics.com: https://secure.ipdanalytics.com/User/Pharma/Biosimilar
11. IPD Analytics. (2021, May 4). Codesource. Bay Harbor Islands, FL, USA. Retrieved from https://codesource.ipdanalytics.com/: https://codesource.ipdanalytics.com/search-results/hcpcs/all/Lucentis
12. IPD Analytics. (2021, February 17). IPD Analytics Market Forecast Update: Herceptin Utilization Expected to Continue to Decline as Biosimilars Gain Market Share. Bay Harbor Islands, FL, USA.
13. IPD Analytics. (2021, March 18). IPD Analytics Market Forecast Update: Outlook for Neulasta and Neulasta Onpro Following Rescheduled Pre-Approval Inspection for Rolontis . Bay Harbor Islands, FL, USA.
14. IPD Analytics. (2021, March 1). IPD Analytics Pharmacy & Therapeutics Watch List | 03.01.2021. Bay Harbor Islands, FL, USA.
15. IPD Analytics. (2021). Market & Financial Insights: Highlights from the J.P. Morgan Annual Healthcare Conference. Bay Harbor Islands, FL: IPD Analytics.
16. Kellaher, C. (2021, August 6). FDA Rejects Spectrum's Rolontis Due to Manufacturing Issues >SPPI. Retrieved from www.marketwatch.com: https://www.marketwatch.com/story/fda-rejects-spectrum-s-rolontis-due-to-manufacturing-issues-sppi-271628250903
17. PR Newswire. (2021, March 31). Evive Biotech Submits Biologics License Application to US FDA for Ryzneuta. Retrieved from apnews: https://apnews.com/press-release/pr-newswire/business-technology-products-and-services-asia-product-testing-445228256c024404d026c1195e8aaa9b
18. US Food & Drug Administration. (2021, May 6). Drug Trials Snapshot: MARGENZA. Retrieved from FDA.gov: https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshot-margenza#:~:text=MARGENZA%20was%20studied%20in%20one%20trial%20that%20enrolled,infusions%20every%20three%20weeks%20in%20addition%20to%20chemotherapy.

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